
Tissue engineering of the intestine in a murine model.

Journal: J Vis Exp

Publication Year: 2012

Authors: Erik R Barthel, Allison L Speer, Daniel E Levin, Frederic G Sala, Xiaogang Hou, Yasuhiro Torashima, Clarence M Wigfall, Tracy C Grikscheit

PubMed link: 23222891

Funding Grants: Mechanism of Tissue Engineered Small Intestine Formation, CHLA Stem Cell Training Grant

Public Summary:

Tissue-engineered small intestine (TESI) has successfully been used to rescue Lewis rats after massive small bowel resection, resulting in return to preoperative weights within 40 days.(1) In humans, massive small bowel resection can result in short bowel syndrome, a functional malabsorptive state that confers significant morbidity, mortality, and healthcare costs including parenteral nutrition dependence, liver failure and cirrhosis, and the need for multivisceral organ transplantation.(2) In this paper, we describe and document our protocol for creating tissue-engineered intestine in a mouse model with a multicellular organoid units-on-scaffold approach. Organoid units are multicellular aggregates derived from the intestine that contain both mucosal and mesenchymal elements,(3) the relationship between which preserves the intestinal stem cell niche.(4) In ongoing and future research, the transition of our technique into the mouse will allow for investigation of the processes involved during TESI formation by utilizing the transgenic tools available in this species.(5)The availability of immunocompromised mouse strains will also permit us to apply the technique to human intestinal tissue and optimize the formation of human TESI as a mouse xenograft before its transition into humans. Our method employs good manufacturing practice (GMP) reagents and materials that have already been approved for use in human patients, and therefore offers a significant advantage over approaches that rely upon decellularized animal tissues. The ultimate goal of this method is its translation to humans as a regenerative medicine therapeutic strategy for short bowel syndrome.

Scientific Abstract:

Tissue-engineered small intestine (TESI) has successfully been used to rescue Lewis rats after massive small bowel resection, resulting in return to preoperative weights within 40 days.(1) In humans, massive small bowel resection can result in short bowel syndrome, a functional malabsorptive state that confers significant morbidity, mortality, and healthcare costs including parenteral nutrition dependence, liver failure and cirrhosis, and the need for multivisceral organ transplantation.(2) In this paper, we describe and document our protocol for creating tissue-engineered intestine in a mouse model with a multicellular organoid units-on-scaffold approach. Organoid units are multicellular aggregates derived from the intestine that contain both mucosal and mesenchymal elements,(3) the relationship between which preserves the intestinal stem cell niche.(4) In ongoing and future research, the transition of our technique into the mouse will allow for investigation of the processes involved during TESI formation by utilizing the transgenic tools available in this species.(5)The availability of immunocompromised mouse strains will also permit us to apply the technique to human intestinal tissue and optimize the formation of human TESI as a mouse xenograft before its transition into humans. Our method employs good manufacturing practice (GMP) reagents and materials that have already been approved for use in human patients, and therefore offers a significant advantage over approaches that rely upon decellularized animal tissues. The ultimate goal of this method is its translation to humans as a regenerative medicine therapeutic strategy for short bowel syndrome.

Source URL: <https://www.cirm.ca.gov/about-cirm/publications/tissue-engineering-intestine-murine-model>